

(FILE 'HOME' ENTERED AT 13:22:25 ON 08 SEP 2000)

09/312351 Search history

FILE 'MEDLINE' ENTERED AT 13:22:33 ON 08 SEP 2000

L1 2 S RNASE AND DISULFIDE AND PKA
L2 6 S PKA(5A)(DISULFIDE OR CYSTINE)
L3 100 S DISULFIDE AND (POLYCATION? OR POLYANION? OR AMPHIPATHIC)
L4 25 S DISULFIDE AND PEG
L5 3 S DISULFIDE AND POLYANION
L6 77 S SOD AND DISULFIDE
L7 17 S TRANSFERRIN AND DISULFIDE AND KINETIC?
L8 0 S L7 AND (INTRAMOLECULAR OR ATTACK)
L9 16 S (PROTEIN FOLDING) AND (DISULFIDE (20A) ACTIVATION)
L10 0 S L9 AND (TRANSFERRIN OR SOD OR SUPEROXIDE)
L11 3 S BPTI AND PEG
L12 15 S (BPTI OR APROTININ) AND (POLYCATION OR POLYANION OR POLYLYSIN
L13 22 S RNASE AND (POLYLYSINE OR (POLY-L-LYSINE) OR POLYCATION)

FILE 'STNGUIDE' ENTERED AT 14:43:35 ON 08 SEP 2000

FILE 'STNGUIDE' ENTERED AT 14:52:31 ON 08 SEP 2000

FILE 'MEDLINE' ENTERED AT 15:07:04 ON 08 SEP 2000

L14 7 S TRANSFERRIN AND FOLDING AND DISULFIDE
L15 29 S (HUMAN TRANSFERRIN) AND DISULFIDE
L16 2 S L15 AND FOLDING
L17 2 S L15 NOT RECEPTOR

(FILE 'HOME' ENTERED AT 16:00:42 ON 08 SEP 2000)

FILE 'MEDLINE' ENTERED AT 16:00:49 ON 08 SEP 2000

L1 17525 S TRANSFERRIN
L2 1 S L1 AND DISULFIDE ISOMERASE

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:01:50 ON 08 SEP 2000

L3 6 S L2
L4 4 DUP REM L3 (2 DUPLICATES REMOVED)

L11 ANSWER 2 OF 3 MEDLINE

AN 96041290 MEDLINE

DN 96041290

TI Characterisation of a novel series of aprotinin-derived anticoagulants. I. In vitro and pharmacological properties.

AU Stassen J M; Lambeir A M; Matthyssens G; Ripka W C; Nystrom A; Sixma J J; Vermeylen J

CS Department of Orthopaedics and Hand Surgery, University of Umea, Sweden.

SO THROMBOSIS AND HAEMOSTASIS, (1995 Aug) 74 (2) 646-54.

Journal code: VQ7. ISSN: 0340-6245.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199605

AB Previous investigations have indicated that interference with the initial level of the blood coagulation may lead to effective antithrombotic therapy. Recently a series of potential coagulation inhibitors derived from bovine pancreatic trypsin inhibitor (BPTI, aprotinin) was described. We have determined their inhibition constants, effects on coagulation assays, effects in an in vitro human thrombosis model and pharmacological profiles in hamsters. The aprotinin-derived analogues (4C2, 7L22, 5L15, 6L15, 5L84) showed significantly increased inhibitory activity towards factor Xa, factor VIIa-tissue factor (TF) complex, factor XIa and plasma kallikrein or a combination of them, and a significantly decreased plasmin inhibition as compared to aprotinin. In the coagulation assays, 4C2 and 7L22 mainly inhibited factor Xa, 5L15 and 6L15 inhibited factor VIIa-TF complex and 5L84 inhibited factor Xa, factor VIIa-TF complex and the contact activation. In flow chamber experiments with human blood 7L22, 5L15, 6L15, 5L84 and rTAP significantly inhibited fibrin formation and platelet deposition on extracellular matrix from phorbol ester stimulated human endothelial cells both under high and low shear stress and in the presence of low molecular weight heparin. The pharmacological profiles of the aprotinin analogues and rTAP with a mean residence time of 64 to 140 min were not significantly different. Modification of an aprotinin analogue with PEG (5L15-PEG) resulted in a 10-fold decrease of the inhibition constant for the factor VIIa-TF complex and in a significant prolongation of the secondary half-life, while the initial half-life was unchanged. (ABSTRACT TRUNCATED AT 250 WORDS)